

85. A method for the detection and extended diagnosis of thrombosis and thrombotic states which comprises labeling the compound of claim 64 with radioactive tracers and using said labeled oligosaccharides in in vivo tests for the detection and diagnosis of thrombosis and thrombotic states.

86. The process of claim 42 wherein the glucosylation reaction is carried out at a temperature above 100°C in the presence of a catalyst.

87. The process of claim 82 wherein the catalyst is 2,6-dimethyl pyridinium perchlorate.

88. A process for the organic synthesis of oligosaccharides which comprises

- reacting a galactosamine or glucosamine with an iduronic or glucuronic acid to form a glycosylation -O-linkage,
- removing at least one acyl group from a position which is inert in the glycosylation reaction to form an OH group,
- reacting the OH group to form an O-sulfate ester or O-phosphate ester and
- removing at least one substituted alkyl group to form a hydroxy group.--

R E M A R K S

Favorable reconsideration of this application is respectfully requested.

There are now 43 claims in this application, claims 41 to 88, claim 41 has been allowed. Claims 42-48 are drawn to the process of making the compounds of the invention and were previously submitted (June 27, 1984 Amendment). They have been amended in view of the Official Action mailed February 15, 1985, as will be discussed below. Claims 49-68 are drawn to the compounds of the invention, claims 69-72 and 81-82 are drawn to the pharmaceutical composition. Claims 73-80 are drawn to the method of use of the pharmaceutical compositions. Claims 83-84 are drawn to conjugates of the compounds, and claim 85 is drawn to a method of use. Claims 86-88 are additional process claims.

The basis for the conjugate claims 83 and 84 is found in the specification on page 50, lines 11-16. Basis for the additional method of use claims 73-80 is found in the specification on page 48, line 11 to page 49, line 12. The basis for the pharmaceutical composition claims 81 and 82 is found on page 49, lines 7-12. The basis for claim 85 is found on page 52, line 10 to page 53 line 8.

This application relates to novel synthetic oligosaccharides which are useful in the treatment of thrombosis, conjugates of the oligosaccharides, pharmaceutical composition comprising the oligosaccharides, the use of the saccharides to detect and treat thrombosis and the process for making these new and useful compounds.

Claims 1-40 and 42-48 are rejected under 35 USC 112, first and second paragraphs for several reasons including being unduly prolix (claims 5, 25 and 30); being functional, indefinite or alternative in the use of several terms; improper use claim (claim 30); being directed to several different processes (claim 14); and having misspelled words (claims 14 and 37).

Claims 1-4 were cancelled without prejudice in the June 1984 Amendment. In this Amendment claims 5-40 have been cancelled without prejudice and replaced by newly presented claims 49-88. The newly presented claims relate to the cancelled claims according to the Table below.

<u>New claim</u>	<u>Prior claim</u>	<u>New claim</u>	<u>Prior claim</u>
49	23		
50	24	68	31
51	25,26,27, 28	69	37
52	25,29,31	70	38
53	25,29	71	39
54	26,29,31	72	40
55	26,29	73	
56	27,29,31	74	
57	27,29	75	
58	28,29,31	76	
59	28,29	77	
60	30	78	
61	30	81	
62	30	82	
63	33	83	
64	34	84	
65	35	85	36
66	35	86	14
67	35	87	14
		88	21

The claims have been rewritten to place the claims in conformance with the requirements of 35 USC 112 first and second paragraphs. Accordingly, 1) the rejected terms have been avoided; 2) the pharmaceutical composition claims (claims 69-72) state the use for which they are intended; 3) claim 36 has been rewritten as a proper use claim (claim 85), 4) claims 25 and 30 have been rewritten, 5) claim 5 has been cancelled without prejudice and 6) an effort has been made to eliminate any misspelled words.

Applicants have noted that the claims to the compounds, pharmaceutical composition and method for use (claims 49-85) have not been rejected under 35 USC 102 and/or 103. Since it is believed that they are also now in conformance with the requirements of 35 USC 112, they are believed to be in condition

for allowance and such action is respectfully requested.

Claims 1-21 and 42-48 are rejected under 35 USC 103 as being unpatentable over each of the patents to Szarek et al, Nair et al, Coussediere et al, the PCT French application or Kochetkov et al reference. This rejection is respectfully traversed.

The Examiner asserts that each of the references discloses the instantly claimed conventional process and that the novelty herein is seen to be in the use of other saccharide reactants. The Examiner states that to "substitute the instant starting materials in the processes shown by each of the references is deemed to be an obvious substitution well within the ordinary skill in the art".

The Examiner's attention is directed to the fact that the process of the invention produces patentable compounds, as she herself has indicated by allowing claim 41. There is no teaching in any of the references cited by the Examiner to combine the processes to obtain the products claimed. As stated in the June 1984 Amendment, this is a highly unpredictable field and it would not be obvious to one skilled in the art that the processes would produce the desired compounds.

Thus, even with using a combination of processes which are shown in the art cited by the Examiner, an unexpected and unobvious result has been obtained.

Furthermore, in claims 86-88 Applicants have further distinguished the process of the invention. Claims 86 calls for the glycosylation reaction to be carried out at a temperature greater than 100°C. Claim 88 calls for the sulfation of hydroxy groups and the subsequent debenzylation of remaining protected hydroxy groups to obtain hydroxy groups in the presence of sulfate groups. There is no teaching or disclosure

in the cited art of a glycosylation reaction carried out at a temperature over 100°C. There is no teaching or disclosure of introducing sulfate groups and subsequently debenzylating other groups to obtain hydroxy groups in the presence of sulfate groups. Thus the processes claimed is not suggested in the prior art.

Accordingly applicants believe the process of the invention is patentable over the cited art and such action is respectfully requested.

Should the Examiner believe that a telephone call to the undersigned or Gerard J. Weiser, attorney of record, would further advance the favorable prosecution of this application or narrow the issues under consideration, she is respectfully invited to call at the telephone number indicated below.

Respectfully submitted,



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Signature
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Date